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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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909	7590	03/16/2006	EXAMINER	
PILLSBURY WINTHROP SHAW PITTMAN, LLP			EPPERSON, JON D	
P.O. BOX 10500			ART UNIT	
MCLEAN, VA 22102			PAPER NUMBER	
			1639	
DATE MAILED: 03/16/2006				

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/743,746

Applicant(s)

SCHMIDT ET AL.

Examiner

Jon D. Epperson

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 November 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-6, 10, 11, 13-31 and 35-39 is/are pending in the application.
- 4a) Of the above claim(s) 3, 13-19, 23-30 and 35-39 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 2, 4-6, 10, 11, 20-22 and 31 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of the Application

1. The Response filed November 8, 2005 is acknowledged.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior office action.

Status of the Claims

3. Claims 1-6, 8, 10-31 and 35-39 were pending. Applicants amended claims 1, 10 and 11. In addition, Applicants canceled claims 8 and 12. Therefore, claims 1-6, 10, 11, 13-31 and 35-39 are currently pending.
4. Claims 3, 13-19, 23-30 and 35-39 are drawn to non-elected species and/or inventions and thus these claims remain withdrawn from further consideration by the examiner, 37 CFR 1.142(b), there being no allowable generic claim. The Examiner notes that contrary to Applicants' assertions (e.g., see 11/8/05 Response, page 9, paragraph 1), claim 13 is also withdrawn from consideration (e.g., see 6/8/05 Office Action, paragraph 1; see also 10/6/04 Office action, paragraph 4; see also 1/5/04 Office Action, paragraph 6).
5. Therefore, claims 1, 2, 4-6, 10, 11, 20-22 and 31 are examined on the merits in this action.

Withdrawn Objections/Rejections

6. The 35 U.S.C. 112, second paragraph rejections are withdrawn in view of Applicants' arguments and/or amendments. The Double Patenting rejections are withdrawn in view of terminal disclaimers. All other rejections are maintained and the arguments are addressed below.

Outstanding Objections and/or Rejections

Claims Rejections - 35 U.S.C. 102 - maintained

7. Claims 1, 2, 4-6, 11, 20 and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Nothnagel (Nothnagel, E. A. "Synthesis and characterization of fluorescent Lucifer yellow-lipid conjugates" *Biochimica et Biophysica Acta* **1989**, 980(2), 209-219).

For *claim 1*, Nothnagel (see entire document) disclose methods for synthesizing and using fluorescent Lucifer yellow-lipid conjugates (see Nothnagel, abstract), which anticipates claim 1. For example, Nothnagel disclose providing a compound in which the analyte is attached by a cleavable linker to a reporter group relatable to the analyte having the formula shown in claim 1 (e.g., see Nothnagel, figure 1, schematic B showing a compound with formula $LY-SO_2-CH_2-CH_2-DC_{12:0}PE$). In this scenario, the Lucifer Yellow Dye ("LY") represents the "reporter" and the $DC_{12:0}PE$ represents the "analyte." In addition, Nothnagel further disclose cleaving the reporter group from the analyte (e.g., see Nothnagel, figure 2 wherein the $DC_{12:0}PE$ "analyte" is cleaved from the LY "reporter" via FAB-MS i.e., the peak at 578 corresponds to the "cleaved" $DC_{12:0}PE$ analyte peak). Please note that the 578 peak corresponds to cleavage between the R' group and the carbon atom β with respect to the sulphone or sulfoxide wherein said β carbon atom is

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proximal to the R' group (e.g., -Ph-SO₂-CH₂-CH₂ ↓NH-). Finally, Nothnagel disclose identifying the reporter group, thereby characterizing the analyte (e.g., see Nothnagel, figure 2 wherein the parent ion and fragment ions that contain the FY reporter are "identified" and used to "identify" the lipid analyte via comparison of molecular weights and known 1:1 correlation between reporter and analyte). Please note that there are many other variations for the analyte and/or reporter that also read on Applicants' claims. For example, the "analyte" could be a "12:0 fatty acid side chain" instead of the DC_{12:0}PE mentioned above or the phosphatidic acid portion ("PA") of the molecule (e.g., see Nothnagel, figure 2 wherein the peaks at 946 and 346 represent "lyso" derivatives of DC_{12:0}PE wherein fatty acid side chain "analytes" are cleaved from the reporter).

For *claim 2*, Nothnagel disclose a covalent linkage between the analyte and/or reporter group and the cleavable linker (e.g., see figure 2 showing the cleavage of a covalent bond when the DC_{12:0}PE signal is generated at mass 578).

For *claim 4-6*, Nothnagel disclose a substituted phenyl wherein R², R⁴, R⁵ and R⁶ are hydrogen and R³ is LY (e.g., see Nothnagel, figure 1, scheme B wherein a phenyl ring connects the LY to the SO₂-CH₂-CH₂-DC_{12:0}PE i.e., LY-phenyl-SO₂-CH₂-CH₂-DC_{12:0}PE).

For *claims 11*, Nothnagel disclose LY-phenyl-SO₂-CH₂-CH₂-N(H)-CH₂-CH₂-DC_{12:0}PA wherein "PA" represents the phosphatidic acid portion of the molecule (e.g., see Nothnagel, figure 1, scheme B). In this scenario, X' is PA, the "handle" connecting PA to N-R¹ is -CH₂-CH₂-, R¹ is hydrogen, the "handle" connecting SO₂ to X is a covalent

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bond and X is LY. Please note that claim 12 has been interpreted as depending on claim 11.

For *claims 20 and 31*, Nothnagel disclose detecting the reporter using FAB-MS and its cleavage products (e.g., see Nothnagel, figure 2).

Response

8. Applicant's arguments directed to the above 35 U.S.C. § 102 rejection were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from its original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

[1] Applicants argue, "Applicants have ... remove[d] the -S- group from the list of possible R' groups. Nothnagel, however, only describes a compound where R' is a thioester (-S-) group. Therefore, Nothnagel fails to teach Applicants' claimed invention (e.g., see 11/8/05 Response, page 9, section II).

[2] Applicants argue, "Nothnagel does not disclose a method for identifying an analyte ... Nothnagel only discloses a method for producing a probe for labeling cell plasma membranes that does not involve identification of an analyte ... Further, there is no suggestion that it would be useful to use such a cleavage as a method of identifying the analyte, and Nothnagel does not disclose the identification of an analyte by identification of a reporter" (e.g., see 11/8/05 Response, page 8, section II).

[3] Applicants argue, “Nothnagel does not disclose the specific step of cleaving the reporter group from the analyte where the compound is cleaved into two parts at a particular point” (e.g., see 11/8/05 Response, page 8, section II).

[4] Applicants argue, “The fragmentation that is observed in the mass spec characterization of the lipid/fluorophores complex ... is incidental to the disclosure; the intention of Nothnagel was not to use the mass spectrometer to analyze one portion as a mass marker to identify the other portion. Therefore, one of ordinary skill in the art would not be motivated by the description of Nothnagel to reach the methods claimed by Applicants” (e.g., see 11/8/05 Response, page 8, section II).

[5] Applicants argue, “Applicants’ claimed invention recites a specific cleavage that is reproducible with other markers. The cleavage that takes place in the molecule disclosed in Nothnagel is neither specific nor reproducible” (e.g., see 11/8/05 Response, page 8, section II).

This is not found persuasive for the following reasons:

[1] This statement appears to be in error as Nothnagel teaches an -NH- group (e.g., see Nothnagel, figure 1), not an -S- group as purported. Consequently, Applicants’ arguments are moot.

[2] The Examiner respectfully disagrees. The cleavage fragments were “identified” in the mass spectra and further used as a “fingerprint” to “identify” the parent ion and/or analyte (e.g., see figure 2).

[3] The 578 cleavage fragment was identified as the [M-H]⁺- for DC12:0PE, which could only form by cleavage of the bond between the R group and the carbon atom in the β position

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with respect to the sulphone or sulfoxide (e.g., see figure 2). thus, Nothnagel does disclose the specific step of cleaving the reporter at the specified location.

[4] Motivation is not an issue for an anticipation rejection. Consequently, Applicants' arguments are moot. In addition, the Examiner notes that the fragmentation in Nothnagel was not "incidental" to the disclosure as purported. The lipid/fluorophores complex was purposefully fragmented using negative-ion fast atom bombardment so that the resulting fragments could be used to identify and/or characterize the parent ion (e.g., see Nothnagel, figure 2 wherein the parent ion and fragment ions that contain the FY reporter are "identified" and used to "identify" the lipid analyte via comparison of molecular weights and known 1:1 correlation between reporter and analyte). Thus, Nothnagel expressly teaches this limitation.

[5] In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., "reproducible" cleavage) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). In addition, the Examiner notes that cleavage of the DC12:OPE is specific (i.e., only occurs at one place) and is also reproducible as this probably represents a "stable" fragment in the mass spec.

Accordingly, the 35 U.S.C. §102 rejection cited above is hereby maintained.

New Rejections

Claims Rejections - 35 U.S.C. 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

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The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1, 2, 4-6, 10, 11, 20-22 and 31 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed had possession of the claimed invention. This is a new matter rejection.

A. Claim 1 was amended in the 11/8/05 Response. However, the Examiner cannot find support for the current amendments in the passages cited by Applicants (e.g., see 11/8/05 Response, page 9, paragraph 1). Specifically, the Examiner only finds support for cleavage between the R' group and the carbon atom in the β position with respect to the sulphone or sulfoxide when the β carbon is "proximal" to the R' group. That is, the specification only supports $\text{-SO}_n\text{-C}(\alpha)\text{-C}(\beta)\text{-}\downarrow\text{R}'$ not, for example, $\text{C}(\beta)\downarrow\text{C}(\alpha)\text{-SO}_n\text{-C}(\alpha)\text{-C}(\beta)\text{-R}'$ or $\text{C}(\beta)\text{-C}(\alpha)\downarrow\text{SO}_n\text{-C}(\alpha)\text{-C}(\beta)\text{-R}'$ both of which occur between the "distal" β carbon and the R'. If applicant believes this rejection is in error, applicant must disclose where in the specification support for this amendment can be found in accordance with MPEP 714.02. Therefore, claim 1 and all dependent claims represent new matter.

Conclusion

Applicant's amendment necessitated any new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO**

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MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D Epperson whose telephone number is (571) 272-0808. The examiner can normally be reached Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jon D. Epperson, Ph.D.
January 24, 2006



ANDREW WANG
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600